

IN THE SPECIFICATION

Please amend the specification as follows:

Please replace **paragraph 27** with the following paragraph:

"FIG. 3 compares a lysostaphin topical cream according to the present invention to ~~BACTROBAN cream~~ BACTROBAN CREAM (2% mupirocin calcium cream) in an *S. aureus* skin infection model;"

Please replace **paragraph 34** with the following paragraph:

"The term "lysostaphin," as used herein, encompasses any enzyme or anti-staphylococcal agent having proteolytic activity, *in vitro and in vivo*, against pentaglycine-containing bridges in the cell wall peptidoglycan of staphylococci. Lysostaphin within the scope of the invention encompass: wild-type lysostaphin and related proteins or anti-staphylococcal agents, lysostaphin mutants, variants, fully synthetic and partially synthetic lysostaphins, and recombinantly expressed lysostaphin proteins. Lysostaphin variants may be generated by post-translational processing of the protein (either by enzymes present in a producer's strain or by means of enzymes or reagents introduced at any stage of the process, or by mutation of the structural gene. Mutations may include site-deletion, insertion, point mutations, domain removal and replacement mutations. Lysostaphin includes, for example, Lysostaphin purified from *S. simulans*, ~~Ambicin L~~ AMBICIN L (recombinant lysostaphin produced in *Bacillus sphaericus* and available from Nutrition 21 (formerly AMBI) of Purchase, N.Y.), and mature Lysostaphin purified from a *Lactococcus lactis* expression system or an *E. coli* expression system, and truncated lysostaphin as set forth in co-pending and commonly owned WO 03/82124, specifically incorporated by reference herein.

Please replace **paragraph 38** with the following paragraph:

"Lantibiotics within the scope of the invention encompass wild-type lantibiotics and the mutants and variants thereof, fully synthetic and partially synthetic lantibiotics, and recombinantly expressed lantibiotics. As with lysostaphin, variants may be generated

by post-translational protein processing or by structural gene mutation. Mutations include site-deletion, insertion, point mutations, domain removal and replacement mutations.

Nisin, for example, includes native nisin purified from *L. lactis*, ~~Ambicin-N~~ AMBICIN N (a purified form of nisin available from Nutrition 21), and mature or variant recombinant nisins such as the over 20 variants generated by replacing lysines with less polar residues available from NIZO Food Research (Netherlands), including nisin variants H27K and H31K."

Please replace **paragraph 40** with the following paragraph:

"The activity of nisin can also be enhanced by formulation with a non-ionic surfactant at concentrations as low as 0.01 wt %. Examples of non-ionic surfactants suitable for use with the present invention include glycerol monolaurate, sucrose esters such as sucrose palmitate, polysorbate 20, TRITON X100 ($C_{14}H_{22}O(C_2H_4O)_n$), Isoceteth-20, ARLASOLVE 200L (80% polyoxyethylene (20), isohexadecyl ether, 20% water), Lauramine oxide, Decylpolyglucose, Phospholipid PTC, MEROXAPOL $((PPG)_x-(PEG)_y-(PPG)_x)$ 105, and the like. Nisin formulations according to the present invention therefore may optionally contain between about 0.01 and about 5.00 wt % of a non-ionic surfactant."

Please replace **paragraph 46** with the following paragraph:

"Excipients include compounds that promote skin absorption, such as dimethyl sulfoxide (DMSO), partial glycerides of fatty acids, and the like, present at levels up to about 10 wt % of the total formula weight. Examples of partial fatty acid glycerides include, but are not limited to IMWITOR 742 (Caprylic/Capric Glycerides) and IMWITOR 308 (Glyceryl Caprylate) available from SASOL North America, Inc. of Houston, Tex. The topical formulations may also optionally include inactive ingredients to improve cosmetic acceptability, including but not limited to, humectants, surfactants, fragrances, coloring agents, emollients, fillers, and the like."

Please replace **paragraph 53** with the following paragraph:

"A suitable emulsifier is SEPIGEL 305 (a combination including about 40% polyacrylamide, about 15% C₁₃-C₁₄ Iso-paraffin, about 5% Laureth-7 and sterile water sufficient to make 100%) (Seppic, Inc., Fairfield, N.J.)), which is an inverse emulsion of polyacrylamide in liquid paraffin. SIMUGEL 600 (Acrylamide/Sodium Acryloyldimethyl Taurate Seppic Copolymer (and) Isohexadecane (and) Polysorbate 80) (Seppic, Inc.) may also be used, which is an inverse emulsion of polyacrylamide. Bactericidal topical cream formulations will contain about 2 and about 8% by weight, and more typically between about 3 and about 5% by weight of an inverse emulsion as the emulsifier. Bactericidal topical lotion formulations will contain between about 1 and about 10% by weight, and more typically between about 3 and about 5% by weight of an inverse emulsion as the emulsifier."

Please replace **paragraph 56** with the following paragraph:

"Typical bactericidal topical cream and lotion formulations include in the aqueous phase as an excipient between about 2 and about 10% by weight of a skin absorption promoter such as DMSO or partial glycerides of fatty acids such as IMWITOR 308 (Glyceryl Caprylate) and IMWITOR 742 (Caprylic/Capric Glycerides), both of which are available from SASOL North America, Inc. IMWITOR 308 is predominantly a glycerin monoester of caprylic acid. IMWITOR 742 is predominantly a blend of mono-, di- and triglycerides of capric and caprylic acids. Typical bactericidal cream and lotion formulations contain as aqueous phase excipients from about 0.25 to about 5% by weight, and more typically from about 1 and about 3% by weight of water soluble ethoxylated partial glycerides of fatty acids, such as SOFTIGEN 767 (PEG-6 caprylic/capric glycerides), which is also available from SASOL North America, Inc."

Please replace **paragraph 57** with the following paragraph:

"According to one embodiment of the present invention a bactericidal cream or lotion formulation is prepared by pre-blending a hard fat such as SOFTISAN ^{[[78]] 378} (glycerin ester of natural vegetable fatty acids, of isostearic acid and of adipic acid) with an emulsifier such as SEPIGEL 305 (a combination including about 40% polyacrylamide, about 15% C₁₃-C₁₄ Iso-paraffin, about 5% Laureth-7 and sterile water sufficient to make

100% (Seppic, Inc., Fairfield, N.J.)) and an ethoxylated partial glyceride of fatty acids such as SOFTIGEN 767 (PEG-6 caprylic/capric glycerides). The pre-blend can be heated slightly to liquify the hard fat at a temperature that will not degrade or denature the anti-infective agent to be added, typically between about room temperature and body temperature, and typically about 30.degree. C. Higher temperatures, up to 100.degree. C. and higher, can be used. However the mixture must then be permitted to cool before any ingredients susceptible to denaturing are added. Water, one or more anti-infective agents and an absorption promoter, if present, are separately pre-blended. The amount of water employed will determine whether the formulation is a cream or lotion. The two pre-blends are then combined with low-shear agitation to form an oil-in-water emulsion."

Please replace **paragraph 82** with the following paragraph:

"*Topical Cream*: The entire preparation was performed at room temperature and with simple hand mixing using a paddle-style weigh bar. 3 g of SEPIGEL 305 (a combination including about 40% polyacrylamide, about 15% C₁₃-C₁₄ Iso-paraffin, about 5% Laureth-7 and sterile water sufficient to make 100% (Seppic, Inc., Fairfield, N.J.))), 8 g of SOFTISAN 378 (glycerin ester of natural vegetable fatty acids, of isostearic acid and of adipic acid), and 2 g of SOFTIGEN 767 (PEG-6 caprylic/capric glycerides) were added to a 250 mL glass beaker and mixed until a homogenous compound was formed, about one minute. Additional samples were prepared with 5 g of IMWITOR 308 (Glyceryl Caprylate) and 5 g IMWITOR 742 (Caprylic/Capric Glycerides), respectively. 77 mL of sterile was then added all at once and mixed slowly until thickening began, about 1 to 2 minutes. The resulting cream was then mixed vigorously for 30 seconds to ensure uniformity and homogeneity. The final 10 mL of water, containing an appropriate amount of drug, was then added to the cream and mixed for 1 to 2 minutes."

Please replace **paragraph 87** with the following paragraph:

"The efficacy of the 0.5% w/w lysostaphin cream was compared to a commercially available 2% mupirocin cream, ~~BACTROBAN cream~~ BACTROBAN CREAM (2% mupirocin calcium cream) (Glaxo SmithKline). On a mole basis there is 100-fold less lysostaphin in a 0.5% w/w cream than there is mupirocin in a 2% cream.

However, the 0.5% w/w lysostaphin cream was far more effective in treating the mouse skin infection than 2% mupirocin cream after two days of 3 applications per day. (FIG. 3). The typical application for ~~BACTROBAN cream~~ BACTROBAN CREAM (2% mupirocin calcium cream) is 3 applications per day for 10 days, within clinical results expected within 3 to 5 days, so it is not entirely unexpected the mupirocin treated infections still show significant bacterial titers after just two day of therapy. In contrast, the lysostaphin cream was able to eradicate infection in one of three animals and reduce titers in the other two animals to fewer than 100 CFUs after two days of therapy, despite using {fraction (1/100)}th the amount of drug compared to mupirocin. These results demonstrate that lysostaphin is not only more potent than mupirocin in the skin infection model, but it also has a more rapid onset of action, factors that may decrease the probability that the lysostaphin-resistant strains of *S. aureus* will arise."

Please replace **paragraph 91** with the following paragraph:

"Example 3 was repeated, except that the DMSO topical cream was replaced with two topical cream samples, one in which the DMSO was replaced with IMWITOR 308 (Glyceryl Caprylate), and one in which the DMSO was replaced with IMWITOR 742 (Caprylic/Capric Glycerides). Lysostaphin in the topical cream reduced skin colonization by about ten-fold, whereas the addition of the IMWITOR absorption enhancers to the cream resulted in virtually the complete clearance of colonized bacteria (FIG. 7)."

Please replace **paragraph 92** with the following paragraph:

"The nisin topical creams of Example 2 were formulated with 5% w/w IMWITOR 742 (Caprylic/Capric Glycerides). The skin of hairless mice was colonized with *S. aureus* as in Examples 3 and 4. The colonized skin was treated three times a day for 2 days. Nisin in this cream reduced skin colonization in a dose-dependent manner and achieved near complete clearance at a 1% w/w dose of nisin (FIG. 8)."